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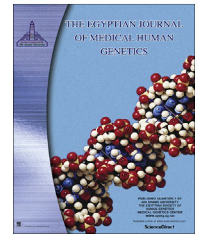

ORIGINAL ARTICLE

Magnesium, zinc and copper estimation in children with attention deficit hyperactivity disorder (ADHD)

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KEYWORDS

ADHD;
Magnesium;
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Abstract *Background:* Attention deficit hyperactivity disorder (ADHD) is a common neuro developmental disorder. Evidence for dietary/nutritional treatments for (ADHD) varies widely, however recommended daily allowance of minerals and essential fatty acids is an ADHD-specific intervention.

Aim of the work: To estimate magnesium, zinc and copper levels in the sera and hair of children with ADHD and compare them to normal children and also to correlate these levels with the disease symptoms.

Methods: This case–control study was conducted on 20 patients with ADHD and 20 age and sex matched healthy controls. All subjects were subjected to psychiatric evaluation according to DSMIV-R, magnesium, zinc and copper estimation in serum and hair follicles. ADHD children were further assessed by the Stanford Binnet intelligence scale for children, Conners' parent rating scale, and Wisconsin's card sorting test.

Results: Magnesium, zinc and copper deficiencies were found in 13 (65%), 14 (60%) and 12 (70%) of ADHD children respectively. Magnesium and zinc deficiencies were found to be correlated with hyperactivity, inattention and impulsivity. However, this correlation was not found in the copper deficient ADHD cases.

Conclusion: Children with ADHD have lower levels of zinc, copper and magnesium compared to both laboratory reference ranges and to normal controls in both hair and serum. These deficiencies are correlated with the core symptoms of ADHD.

1. Introduction

ADHD is a chronic debilitating psychiatric illness that often co-occurs with other common psychiatric problems. Although empirical evidence supports pharmacological and behavioral treatments, side effects and concerns regarding safety and fears

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about their long-term use contribute to families searching for alternative methods for treating the symptoms of ADHD [1].

According to Wilson [2]; calcium, magnesium and zinc are deficient on the tissue mineral analyses of many ADHD children. Supplementation with these minerals alone may occasionally end the hyperkinetic behavior.

Zinc deficiency has an important role in the pathogenesis of ADHD [3]. Zinc is an important cofactor for metabolism relevant to neurotransmitters, prostaglandins, and melatonin, and indirectly affects dopamine metabolism [4]. It mediates the release of neurotransmitters like gamma amino butyric acid [GABA] and glutamate. This indicates that it may be a key modulator of neuronal excitability [5]. Also, zinc is an important cofactor for more than 300 other nutrients. So, zinc deficiency may create functional deficiency of these other nutrients [6]. These functions have been shown to be affected by moderate zinc deficiencies in humans [7]. Several data suggest that zinc deficiency may be more concentrated in the ADHD population [7]. It, also, seems likely that zinc supplementation in zinc-deficient ADHD patients improves the binding status of the dopamine transporter [8].

Magnesium deficiency is typified by a number of reductions in cognitive ability and processing, and in particular a reduced attention span along with increased aggression, fatigue and lack of concentration [9]. Other common symptoms of magnesium lack include becoming easily irritated, nervousness, fatigue and mood swings [10]. Given the nature of these symptoms and the significant amount of overlap that they share with ADHD, this has led many experts involved in the treatment and care of ADHD to hypothesize that children who suffer from the condition also have magnesium deficiency as well [11]. Moreover, magnesium helps in generating ATP and energy [11], disposing brain ammonia, which is related to inattention [12] and converting essential fatty acids into DHA (docosahexaenoic acid), which is related to proper function and structure of brain cells [12]. It has an antioxidant effect, where it can decrease the oxidative stress related to pathophysiology of ADHD [13]. Moreover, magnesium can improve sleep disturbance seen in ADHD [14] which may adversely affect the attention.

Copper is an essential factor for both development and function of the central nervous system [15]. It acts as a cofactor for several key enzymes, most notably dopamine B-hydroxylase which catalyzes the conversion of dopamine to norepinephrine [16]. Copper is needed in trace amounts, but excess is toxic. Excess copper increases lipid peroxidation and depletes glutathione reserves, which makes the organism more vulnerable to oxidative challenges [15]. Zinc to copper ratio is abnormally low in individuals with disorders associated with hyperactivity. Low zinc may be associated with ADHD [16] and has been directly related to low Cu/Zn Superoxide dismutase (SOD) concentration. Hurt et al. [17] showed that a decreased serum Cu/Zn SOD may be also associated with high copper in children with ADHD.

This paper was done to examine the hypothesis that there are trace element deficiencies in Egyptian patients with ADHD and that these deficiencies may lead to worsening of the disease symptoms.

2. Subjects and methods

This case–control study was conducted on 20 patients with ADHD and 20 age and sex matched healthy controls.

2.1. Participants

We evaluated 50 children (age range 6–16 years) chosen randomly from our Child and Adolescence Psychiatry Clinic, Children Hospital, Ain Shams University who had a diagnosis of ADHD. Twenty patients were found eligible to be included in the study. Patients were considered eligible for the study if they fulfilled criteria of ADHD according to DSMIV-R, had an age range between 6–16 years and an IQ above 70. Ineligibility for the study included presence of other medical conditions such as significant anemia, chronic illness, hearing or vision impairment or medications side effects which may result in hyperactivity and/or impaired sleep rhythm.

Twenty healthy children gathered from the outpatient clinic were included in the study as controls. These children were visiting the outpatient clinic suffering from minor acute illness (common cold, pharyngitis, etc...). Psychiatric assessment was done for all control participants to exclude ADHD and other developmental conditions. This study was approved by the Ethics Committee of Ain Shams University and written consents were obtained from parents. The work has been carried out in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

2.2. Methodology

Each patient in this study was subjected to the following; full detailed medical history; including presence of organic or psychological diseases, perinatal and developmental history, family history of similar cases, and the history of previous treatment which was received and Clinical Examination including; physical examination and neurological examination.

Psychometric evaluation was performed by a trained psychologist for both cases and controls.

- Diagnostic and Statistical Manual, fourth edition-Revised (DSM-R IV) criteria [18] to confirm the diagnosis of ADHD in cases and to exclude concomitant psychiatric disease.
- Conners' parent rating scale [19] Items were scored on 14 subscales but in our study we used only the hyperactivity, inattention, oppositional and impulsivity scores.
- Wisconsin's card sorting test (WCST) [20] is a neuropsychological test of "set-shifting", i.e. the ability to display flexibility in the face of changing schedules of reinforcement. It's a measure of executive function.
- Stanford–Binet Intelligence scale [21] shows that the intelligence quotient or IQ is simply the ratio of mental age (MA) to chronological age (CA) multiplied by 100: $IQ = MA/CA \times 100$.

2.3. Laboratory investigations

- Serum magnesium, zinc and copper levels were assayed by auto analyzer and compared to the reference value for normal children [22].
- Hair magnesium, zinc and copper [23] these samples were collected from cases and controls by single cutting from the occipital region. The hair was cut to lengths of about

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1.5–2 cm using clean stainless steal scissors. A minimum of 5–10 mg of hair was required for the hair analysis assay. Approximately 100 strands of hair (50 mg) were used. The hair sample was subjected to Inductively Coupled Mass Spectroscopy (ICP–MS) which has been cited as currently the most sensitive and comprehensive technique available for multi-element analysis of trace elements to measure hair magnesium, zinc and copper in both cases and controls.

2.4. Statistical analysis

The collected data were revised, coded, tabulated and introduced to a computer using Statistical package for Social Science. (SPSS 15.0.1 for windows; SPSS Inc., Chicago, IL, 2001). Data were presented and suitable analysis was done according to the type of data obtained for each parameter.

– For the descriptive statistical analysis of the subjects' demographic data (mean, standard deviation (±SD) we used the Student *t*-test to assess the statistical significance of the difference between two study group means.
– For the analytical statistical analysis many tests were used:
  - For the cutoff values of hair Mg, Zn and Cu in ADHD patients we used the Receiver operating characteristics (ROC) curve as there's no available reference in Egypt for hair trace elements in this age group. Therefore, and according to the (ROC) the best cut off values for magnesium was ⩾58.20 mg/kg, zinc was ⩾108.90 mg/kg and copper was ⩾59.70 mg/kg. The ROC curve provides a useful way to evaluate the sensitivity and specificity for quantitative diagnostic measures that categorize cases into one of two groups.
  - We used Paired *t*-test to compare between patients and control as regards serum magnesium; copper and zinc with referral to standard reference values and also for comparison between cases with normal and low hair and serum trace elements as regards the different psychiatric scales.
  - Paired *t*-test is used to assess the statistical significance of the difference between two means measured twice for the same study group.
  - Chi square test was used to compare between patients and control as regards frequency of Mg, Zn and Cu deficiency in the hair of ADHD patients according to the cut off values. Chi square test is used to examine the relationship between two qualitative variables.
  - Correlation analysis (using Pearson's method) was used to assess correlation between hair trace elements and the patients' psychiatric scales. The correlation analysis assesses the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "*r*" defines the strength and direction of the linear relationship between two variables.

5. Results

This study included 20 ADHD patients and 20 controls. The patients were 16 (80%) males and 4 (20%) females. Their mean age was 7.74 ± 1.48 SD. The mean number of siblings was 1.6 ± 1.3 SD and the mean order of birth was 1.9 ± .9 SD. Three of our patients were the result of consanguineous marriage and 17 were not. Five had family history of mental retardation and 2 of autism. There was no statistically significant difference between patients and controls as regards age and gender i.e. both samples were homogenous. Also, there was no statistically significant difference between both groups as regards the number of siblings, order of birth or family history Table 1.

Children with ADHD had lower levels of serum magnesium, copper and zinc compared with controls (Table 2), and a significant proportion of children's levels of magnesium, copper and zinc were below the cut-off value for reference ranges compared with controls, suggesting deficiency in these nutrients (Table 2). Magnesium levels were highly significantly lower (1.62 ± 0.48 mEq) in patients compared to the levels

Table 1 Statistical comparison between cases and controls as regards the personal characteristics.

		Type				P^*	Sig
		Cases $N = 20$		Controls $N = 20$			
			%		%		
Sex	Male	16	80.00%	10	50.00%	.107*	NS
	Female	4	20.00%	10	50.00%		
Age	Mean ± SD	7.74 ± 1.48		7.40 ± 1.35		.534**	NS
Number of sibling	Mean ± SD	1.6 ± 1.3		1.7 ± .7		.700**	NS
Order of birth	Mean ± SD	1.9 ± .9		1.8 ± .9		.840**	NS
Consanguinity	Negative	17	85%	15	75%	.999*	NS
	Positive	3	15%	5	25%		
Family history	Non	13	65%	12	60%	.434*	NS
	ADHD	0	0%	3	15%		
	Autism	2	10%	1	5%		
	Epilepsy	0	0%	0	0%		
	MR	5	25%	2	10%		

NS = non significant. Sig = significance.
SD = standard deviation; MR = mental retardation; N = number.
* Chi square test.
** Student *t* test.

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Table 2 Statistical comparison between patients and control as regards serum magnesium; copper and zinc with referral to standard reference values.

Parameters	Patients		Control		t-test	
	Mean	SD	Mean	SD	*t*	*P*-value
Serum Mg Meq/L (1.7–2.1 MEq/L)	1.62	0.48	2.56	0.57	−4.715	< 0.001**
Serum Cu ug/dl (90–190 ug/dl)	92.52	57.54	189.89	20.64	−5.150	< 0.001**
Serum Zn ug/dl (70–120 ug/dl)	69.68	22.90	159.54	19.16	−10.658	< 0.001**

Student *t*-test.
SD = standard deviation.
** Highly significant.

Table 3 Statistical comparison between patients and control as regards frequency of Mg, Zn and Cu deficiency in the hair of ADHD patients according to the cut off values.

Trace element	Groups					
	Patients		Controls		X^2	*P* value
	N	%	*N*	%		
Magnesium						
Below cut off value (Mg/kg)	13	65.0	2	10.0	11.471	< 0.001**
Above cut off value (Mg/kg)	7	35.0	18	90.0		
Zinc						
Below cut off value (Mg/kg)	14	70	2	10	9.600	0.002**
Above cut off value (Mg/kg)	6	30	18	90.0		
Copper						
Below cut off value (Mg/kg)	12	60	4	20	4.286	0.038*
Above cut off value (Mg/kg)	8	40	16	80		

Chi-square.
Mg/kg = Magnesium per kilogram.
** Highly significant.
* Significant.

Table 4 Comparison between cases with normal and low hair and serum magnesium as regards different psychiatric scales.

Parameters		Magnesium					
		ADHD patients with low Mg (*n* = 13)		ADHD patients with normal Mg (*n* = 7)		t-test	
		Mean	SD	Mean	SD	*t*	*p*-value
	Age	9.08	2.36	7.71	0.49	1.492	0.153
Verbal skills	Comprehension	10.38	2.66	9.57	2.07	0.699	0.493
	Arithmetic	7.77	2.86	9.29	3.40	−1.060	0.303
	Similarities	11.23	3.27	24.71	35.48	−1.392	0.181
	Digit span	5.23	0.83	5.43	0.79	−0.516	0.612
Performance scale	Picture completion	9.31	3.28	9.57	1.99	−0.193	0.849
	Block design	9.08	3.04	9.14	1.68	−0.053	0.958
	Digit symbols	4.85	1.41	5.43	1.13	−0.941	0.359
	Verbal IQ	96.08	12.30	97.71	11.51	−0.290	0.775
	Performance IQ	89.15	14.98	91.14	7.43	−0.327	0.747
	Total IQ	91.69	14.19	94.86	9.84	−0.523	0.607
Conners' scale	Oppositional	81.46	5.95	69.00	2.52	5.240	0.002
	Inattentional	79.38	2.53	69.43	2.64	8.267	0.004
	Hyperactivity	80.38	6.71	68.43	2.44	4.505	< 0.001
	Impulsivity	81.38	5.50	69.86	1.86	5.324	0.005
WCEST	Category comp.	2.22	1.09	4.50	0.55	−4.686	0.009
	Conceptual level	34.61	15.01	63.58	4.75	−4.529	0.002

Student *t*-test.
SD = standard deviation; *n* = number.

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in controls (2.56 ± 0.58 mEq) with $P = <0.001$. Also, zinc levels were highly significantly lower (69.68 ± 22.9 ug/dl) in patients compared to levels in controls (159.54 ± 19.16 ug/dl) with $P = <0.001$. As for copper levels, they were also highly significantly lower (92.52 ± 57.54 ug/dl) in patients compared to levels in controls (189.89 ± 20.64 ug/dl) with $P = <0.001$.

The number of ADHD patients below the hair trace elements cutoff values was significantly higher than those in controls (Table 3). The number of patients below the hair magnesium cutoff values was 13 patients in comparison to only 2 controls ($P = <0.001$). While, the number of patients below the hair zinc cutoff values were 14 patients as compared to only 2 controls ($P = 0.002$). As for the hair copper, there were 12 patients below cutoff values as compared to 4 controls ($P = 0.038$).

Therefore, and according to these serum reference values and hair cut off values of magnesium, zinc and copper. The

Table 5 Statistical comparison between cases with normal and low hair and serum zinc as regards different psychiatric scales.

Parameters		Zinc					
		ADHD patients with low Zn ($n = 14$)		ADHD patients with normal Zn ($n = 6$)		*t*-test	
		Mean	SD	Mean	SD	*t*	*p*-value
	Age	9.00	2.29	8.81	1.97	0.241	0.811
Verbal skills	Comprehension	10.50	2.59	9.17	1.94	1.124	0.276
	Arithmetic	8.21	3.21	8.50	2.95	−0.186	0.854
	Similarities	11.29	3.15	26.83	38.38	−1.562	0.136
	Digit span	5.29	0.83	5.33	0.82	−0.119	0.907
Performance scale	Picture completion	9.57	3.30	9.00	1.41	0.404	0.691
	Block design	9.14	2.93	9.00	1.79	0.110	0.914
	Digit symbols	4.93	1.38	5.33	1.21	−0.620	0.543
	Verbal IQ	97.14	12.48	95.50	10.86	0.279	0.783
	Performance IQ	90.07	14.80	89.33	6.22	0.116	0.909
	Total IQ	92.79	14.23	92.83	9.04	−0.008	0.994
Conners' scale	Oppositional	80.86	6.15	68.33	1.97	4.817	0.005
	Inattention	78.93	2.97	68.83	2.32	7.372	0.001
	Hyperactivity	79.79	6.83	67.83	2.04	4.150	<0.003
	Impulsivity	80.64	5.97	69.67	1.97	4.345	0.006
WCEST	Category comp.	2.40	1.17	4.60	0.55	−3.927	0.007
	Conceptual level	37.85	17.47	62.90	4.97	−3.091	0.002

Student *t*-test.
SD = standard deviation; *n* = number.

Table 6 Statistical comparison between cases with normal and low hair and serum copper as regards different psychiatric scales.

Parameters		Copper					
		ADHD patients with low Cu ($n = 12$)		ADHD patients with normal Cu ($n = 8$)		*t*-test	
		Mean	SD	Mean	SD	*t*	*p*-value
	Age	9.00	2.09	8.00	1.85	1.095	0.288
Verbal skills	Comprehension	9.92	3.09	10.38	1.06	−0.401	0.693
	Arithmetic	7.58	3.06	9.38	2.92	−1.305	0.208
	Similarities	11.67	2.31	22.38	33.59	−1.116	0.279
	Digit span	5.08	0.90	5.63	0.52	−1.533	0.143
Performance scale	Picture completion	9.33	3.31	9.50	2.14	−0.125	0.902
	Block design	8.67	3.06	9.75	1.67	−0.911	0.374
	Digit symbols	4.92	1.31	5.25	1.39	−0.544	0.593
	Verbal IQ	94.92	12.80	99.25	10.22	−0.800	0.434
	Performance IQ	88.42	14.64	92.00	9.44	−0.610	0.549
	Total IQ	90.58	14.04	96.13	10.19	−0.958	0.351
Conners' scale	Oppositional	77.08	6.07	77.13	10.45	−0.011	0.991
	Inattention	76.33	4.74	75.25	6.73	0.424	0.677
	Hyperactivity	76.00	6.13	76.50	10.77	−0.133	0.896
	Impulsivity	76.92	5.48	78.00	9.65	−0.321	0.752
WCEST	Category comp.	3.18	1.17	3.00	2.31	0.206	0.840
	Conceptual level	47.73	17.03	42.00	25.43	0.508	0.620

Student *t*-test.
SD = standard deviation; *n* = number.

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magnesium deficient patients were found to be 13 (65%), zinc deficient patients were 14 (70%) and copper deficient patients were 12 (60%).

This study showed that there was a significant increase in the oppositional, inattention, hyperactivity and impulsivity components of the Conners Score, and also in the Category Completion and Conceptual component of the Wisconsin scale in cases with normal when compared to cases with deficient magnesium and zinc (Tables 4 and 5). However, there was no such significant difference in the copper deficient cases (Table 6).

Correlation results showed that there was a significant positive correlation between hair magnesium and zinc levels and the inattention, hyperactivity and impulsivity components of the Conners Score. On the other hand there was no significant correlation between copper levels and the different psychiatric scales Figs. 1 and 2.

As for the correlation between serum magnesium and zinc and the inattention, hyperactivity and impulsivity components of the Conners score it was also positive and again there was no significant correlation between serum copper and the different psychiatric scales Figs. 3 and 4.

6. Discussion

In our study ADHD patients were deficient in magnesium, zinc and copper in both hair and serum samples. The levels of these

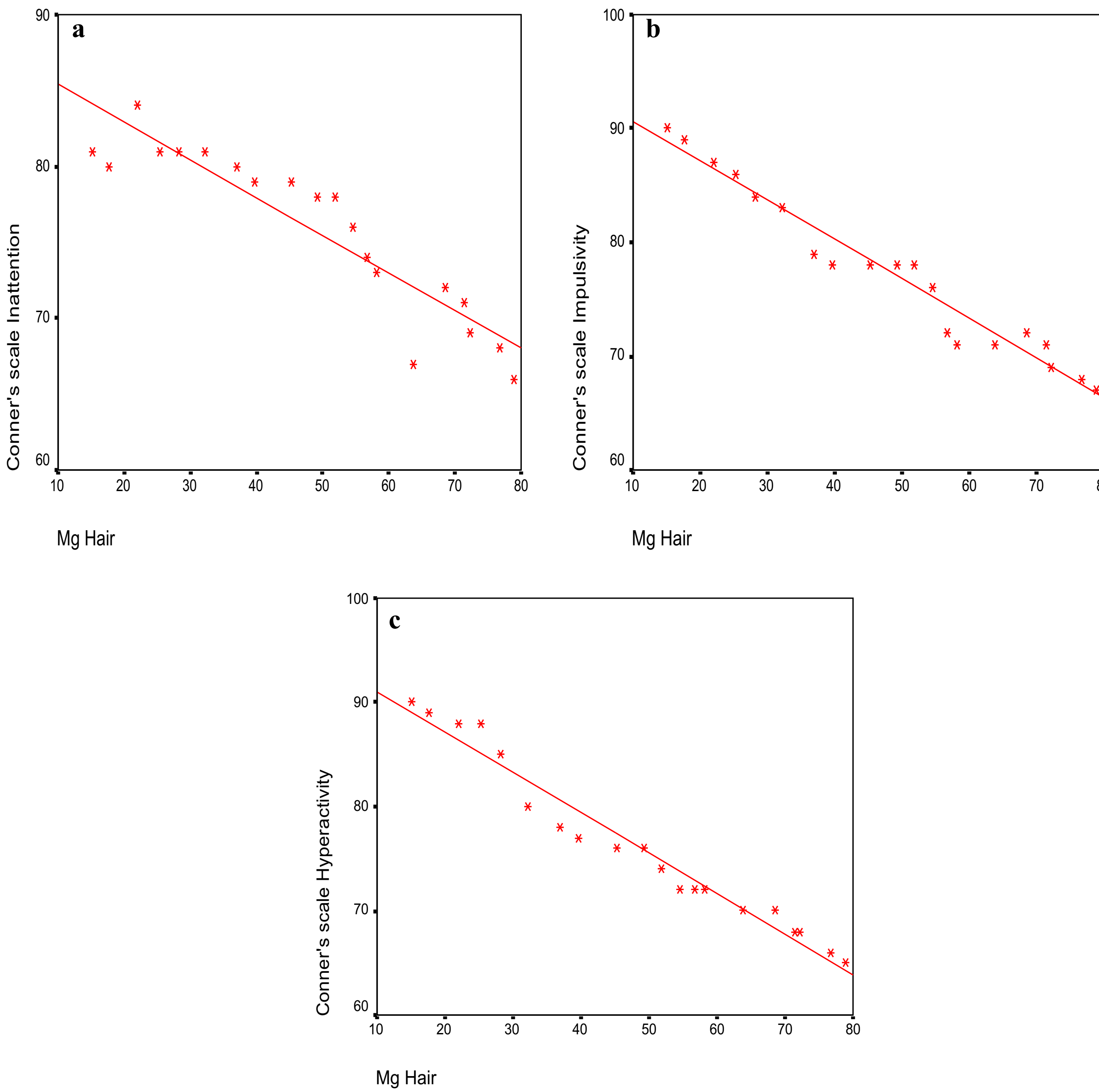

Figure 1 (a–c): Scatter diagram for correlation between hair magnesium level and inattention, impulsivity and hyperactivity components of the Conners scale among children with ADHD showing a significant positive correlation.

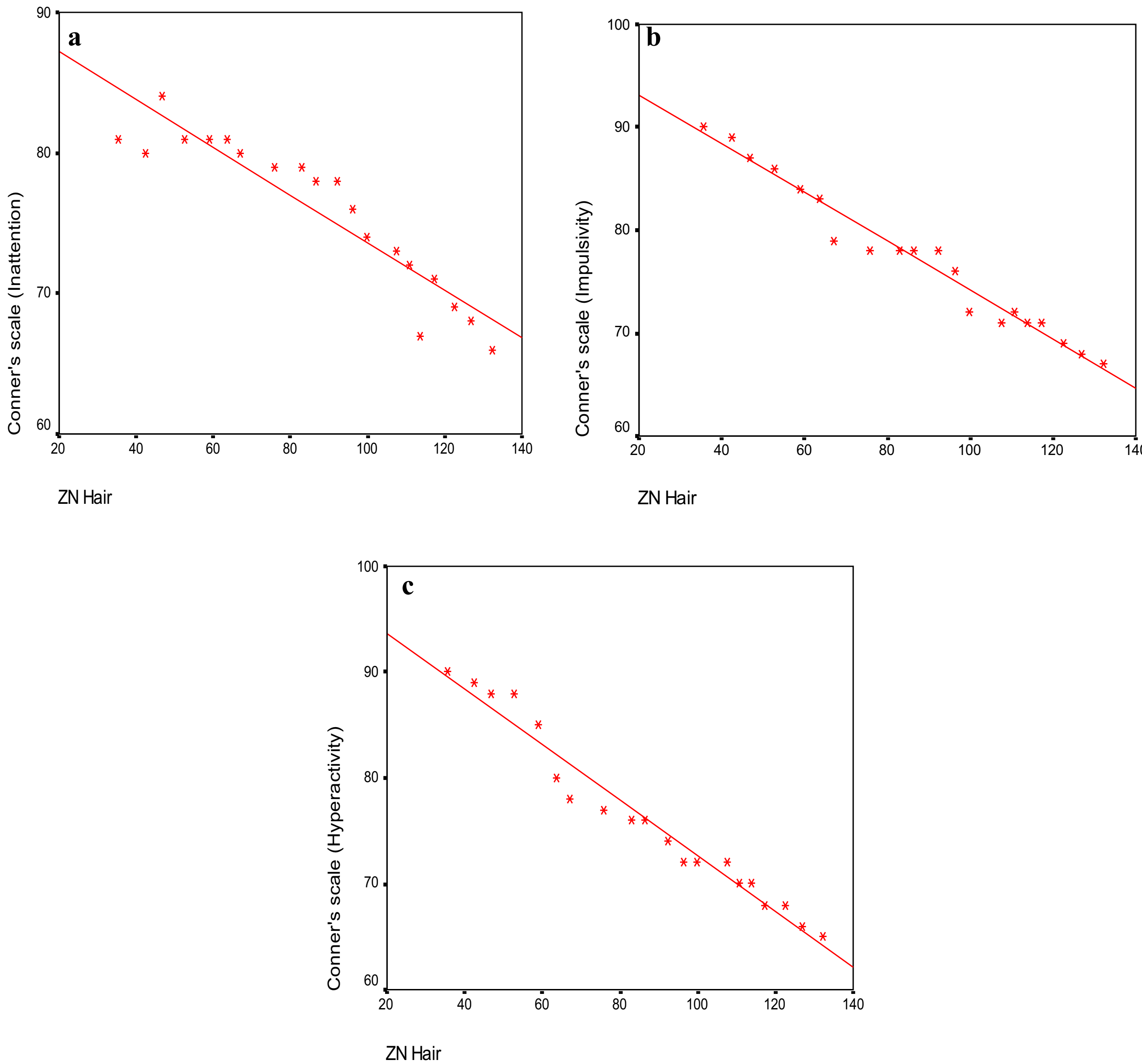

Figure 2 (a–c): Scatter diagram for correlation between hair zinc level and inattention, impulsivity and hyperactivity components of the Conners scale among children with ADHD also showing a significant positive correlation.

trace elements were significantly lower than both laboratory reference ranges and levels in normal controls in both hair and serum.

We can speculate that the trace element deficiency in ADHD patients may be an outcome of behavioral manifestations related to the core pathology of ADHD. Children with ADHD may suffer from feeding problems owing to their stubbornness and unexpected reactions to their parent's orders. Also they lack the attention required to sit through a meal to obtain adequate levels of nutrient intake [24]. It may also be due to the appetite suppressant effects of treatment medication [25]. The deficiencies could also be due to a wide range of other factors including suboptimal nutrition during pregnancy, metabolic abnormalities, gut dysbiosis leading to nutrition mal absorption and other causes of malabsorption. For example Niederhofer [26] reported that Celiac disease is markedly overrepresented among patients presenting with ADHD.

Our results of multiple trace element deficiency in ADHD patients were an area of concern in many studies. For example, the finding of magnesium deficiency in ADHD children came in agreement with a study done by Kozielec [27] where magnesium deficiency was found in 95% of those examined, most frequently in hair (77.6%), in red blood cells (58.6%) and in blood serum (33.6%). Similar results were obtained from 2 Egyptian studies; Mahmoud et al. [28] found that serum ferritin, zinc and magnesium were lower in ADHD children than norms. And ElBaz et al. [29] found hair magnesium deficiency was detected in 72% of ADHD Egyptian children.

As for the deficiency of the trace element zinc seen in our study, it was similar to the results obtained by Kozielec [27]

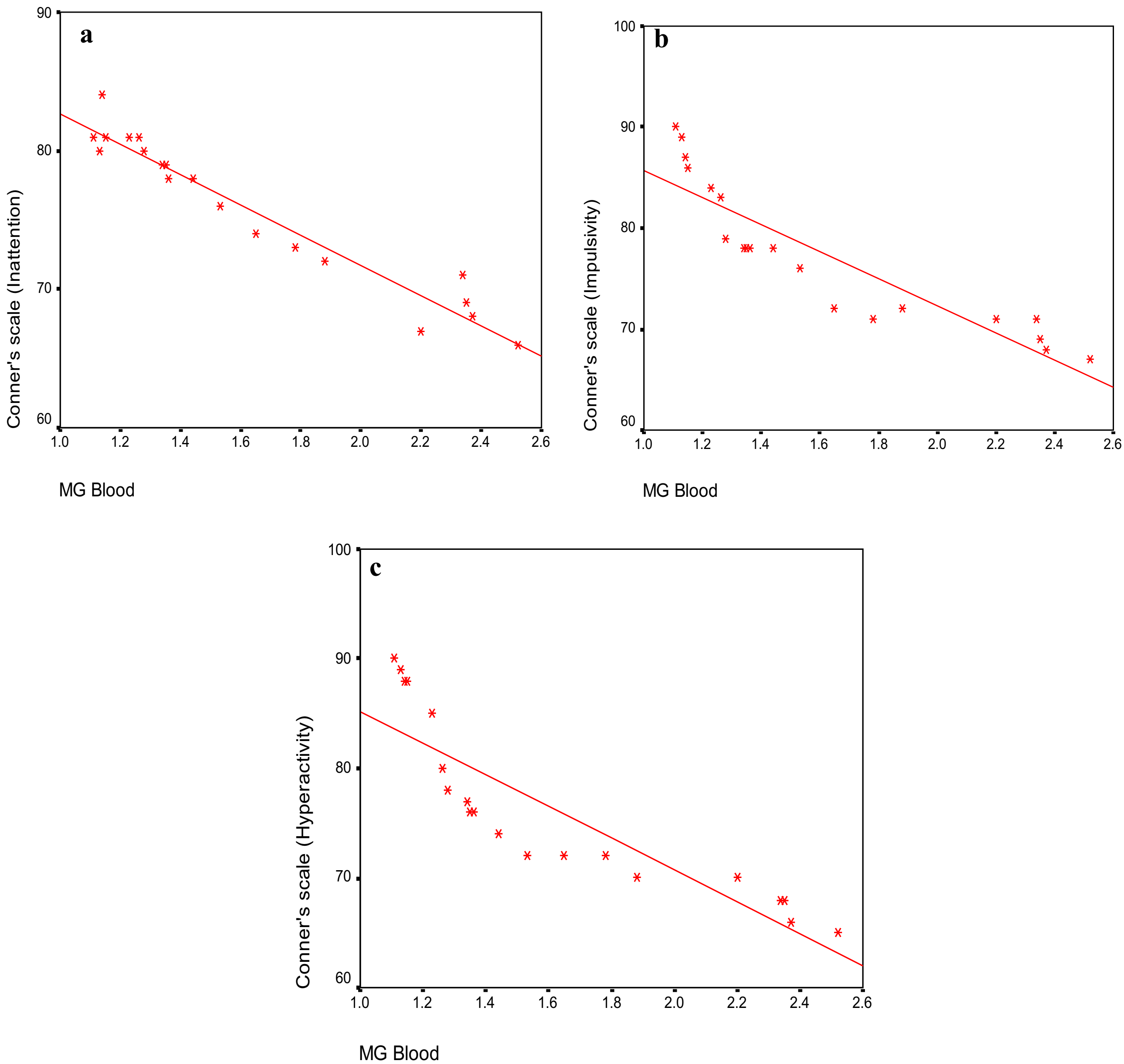

Figure 3 (a–c): Scatter diagram for correlation between serum magnesium and inattention, impulsivity and hyperactivity components of the Conners scale among children with ADHD showing a significant positive correlation.

in Poland and Bekarogluet et al. [30] in Turkey. Arnold et al. [31] reported that 118 children with ADHD had 30% lower 24-h urine zinc than normal controls, suggesting either lower dietary intake or poorer absorption rather than zinc-wasting metabolism.

Moreover, there is also, deficiency of copper seen in the current study which comes in concordance with Joy et al. [32]. On the contrary there are other data suggesting that excess copper has a role in pathogenesis of ADHD [17].

Another Polish study [33] found a high rate of magnesium, zinc, iron, copper and calcium deficiencies in 116 children with ADHD on the basis of serum, red cell and hair analyses.

The finding of significant difference in the Conners scale in the magnesium and zinc deficient cases denotes that the deficiency of these trace elements is implicated in worsening of the symptoms of the disease.

Previous studies demonstrated the effects of magnesium on learning and memory in humans and its deficiency was associated with deficient cognitive function and low academic achievement in adolescent girls [34]. Moreover, familial hypomagnesemia was related to inattention, mental retardation and speech problems [35]. The highly significant increase seen in hyperactivity could also be due to the fact that magnesium is needed for relaxation at neuromuscular junctions [36].

Our results match those obtained by Nogovitsina & Levitina, and Mousain-Bosc, [37,38,39] where magnesium supplementation showed improvement in decreased attention, hyperactivity and anxiety in ADHD children. When the Mg

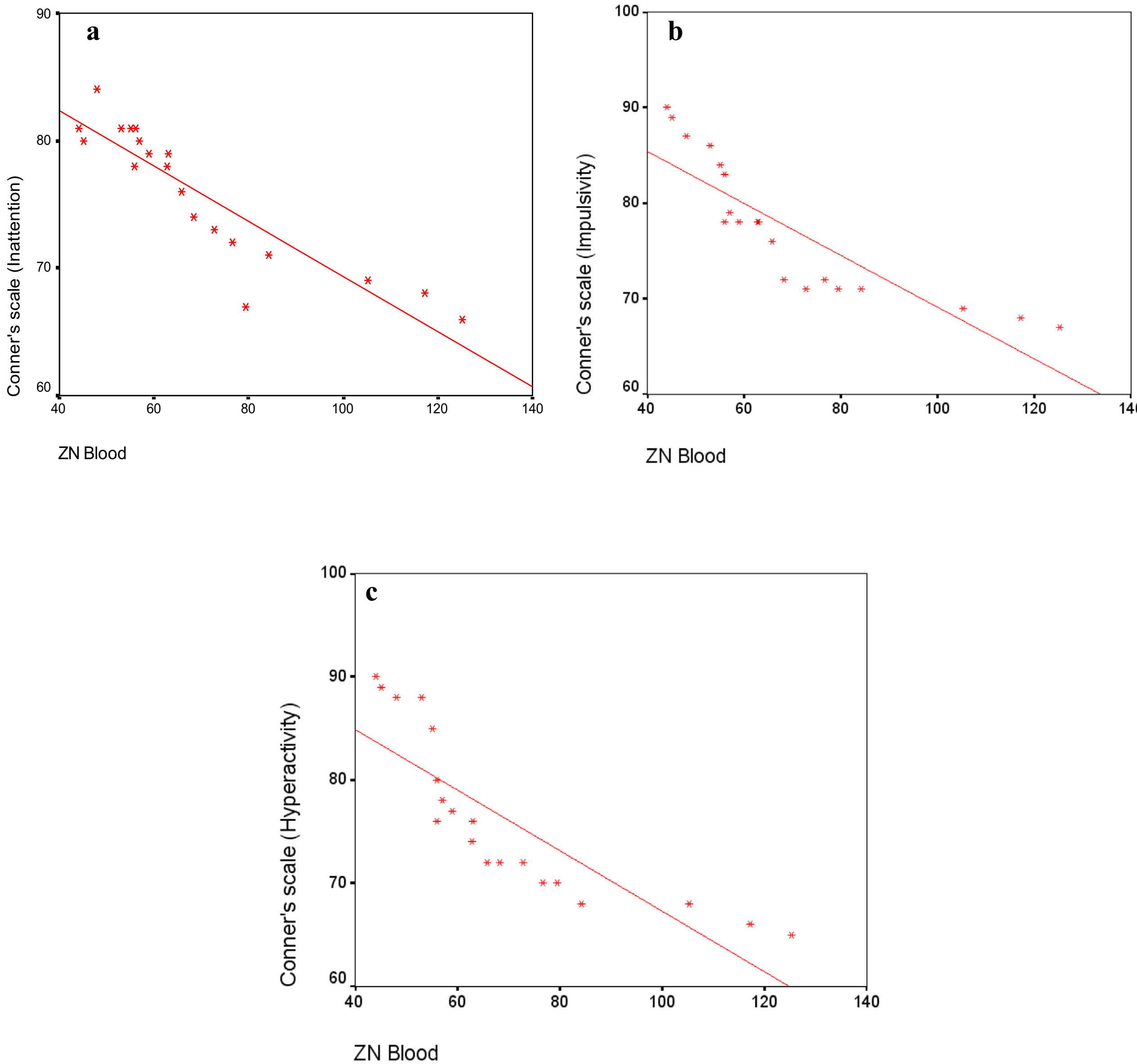

Figure 4 (a–c): Scatter diagram for correlation between serum zinc and inattention, impulsivity and hyperactivity components of the Conners scale among children with ADHD also showing a significant positive correlation.

treatment was stopped, these symptoms reappeared in a few weeks.

In Egypt a study was done by ElBaz et al. [29] and found that magnesium deficiency was detected in 72% of ADHD Egyptian children, supplementation with Mg significantly improved hyperactivity and inattention.

Regarding the results involving zinc level and the patients' different psychiatric scale, zinc deficiency affects cognitive development by alterations in attention, activity, other features of neuropsychological behavior and motor development [5]. Therefore, children with low zinc levels may be at increased risk for ADHD. Akhondzadeh and colleagues [40] examined the effect of zinc supplementation in Iranian children with ADHD, supplemented patients improved significantly more than those assigned to placebo. Also, Arnold et al. [31] reported a significant correlation of baseline hair zinc with Conners' hyperactivity and inattention index in 18 boys with ADHD.

These results suggest that magnesium and zinc supplementation, or at least proper amounts of them in the diet, may prove to be beneficial for children with ADHD.

Regarding the mineral copper our study showed that copper deficiency did not correlate with any of the patients' data and did not have an effect on their psychiatric evaluation. We searched the literature and did not find many papers discussing this particular issue. However, Harris [41] reported that excess copper was associated with hyperactivity and inattention and chelation leads to a significant improvement.

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An interesting finding in our study was the significant difference between ADHD patients with normal and deficient magnesium and zinc levels (not copper) as regards the Category Completion and Conceptual component of the Wisconsin card sorting test (WCST).

The WCST, relies upon a number of cognitive functions including attention, working memory, and visual processing. It measure frontal lobe dysfunction [20].

Our finding that magnesium deficiency leads to impairment of the cognitive functions in ADHD patients came in concordance with a study done by ElBaz et al. [29] where the magnesium deficient ADHD patients had lower scores in the WCST than the non-deficient ones. Magnesium supplementation improved the scores.

Magnesium seems to be one of the most promising compounds to treat people with loss of cognitive function as measured by WCST [42,43].

As for the trace element zinc, a study done by Hambidge & Krebs [5] concluded that zinc deficiency affects cognitive development by alterations in attention, activity and other features of neuropsychological behavior. Therefore, children with low zinc levels may be at increased risk for ADHD.

In Conclusion many children with ADHD have lower levels of zinc, magnesium and copper compared to both laboratory reference ranges and normal controls.

Because our study showed that ADHD patients deficient in zinc and magnesium show more hyperactivity, impulsivity and inattention than those with normal levels, we may speculate that these deficiencies may be incriminated as a contributing factor leading to this behavioral disorder, or may at least play a role in worsening of the symptoms.

These findings lead naturally to the hypothesis that improving zinc and magnesium nutritional status might improve ADHD symptoms or might even lead to amelioration of the disease.

Conflict of interest

The authors declare that they have no competing or potential conflict of interest. There is no financial and personal relationship with other people or organizations that could inappropriately influence their work.

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